

**ATTORNEY DOCKET NO.: 0492611-0315 (MIT 6196)**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant:	Griffith-Cima, et al.	Examiner:	D. Naff
Serial No.:	09/008,945	Art Unit:	1651
Filed:	January 20, 1998		
For:	TISSUE FORMATION BY INJECTING A CELL-POLYMERIC SOLUTION THAT GELS IN VIVO		

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**DECLARATION UNDER 37 C.F.R. 1.132**

We, Anthony Atala, Linda G. Griffith, Charles A. Vacanti, and Keith T. Paige declare as follows:

1. We are the inventors of the subject matter disclosed and claimed in United States patent application Serial No.09/008,945 ('945 application) filed January 20, 1998 and entitled "TISSUE FORMATION BY INJECTING A CELL-POLYMERIC SOLUTION THAT GELS IN VIVO". This application claims priority to United States patent application Serial No. 08/056,140 now issued U.S. Patent No. 5,709,854, by Griffith-Cima et al. entitled "Tissue Formation by Injecting a Cell-Polymeric Solution that Gels In Vivo", filed on April 30, 1993.

2. This Declaration is presented for the purpose of removing from consideration by the Examiner an abstract by Atala et al., entitled "Cartilage Cells as a Potential Treatment for Reflux", American Academy of Pediatrics, 1992 Annual Meeting, Section on Urology Program for Scientific Sessions, San Francisco, CA, Saturday, October 10-12, (1992) (Reference "R"). The conference began on October 10, 1992, at which time the above-referenced abstract was available to the public in this country. The present Declaration is presented in accordance with

*Ex Parte Magner*, 133 USPQ 404 (CCPA 1961) and *In re Katz*, 215 USPQ 14, 18 (CCPA 1982) and establishes that the allegedly anticipatory material in Reference R was not invented by another.

3. Charles Vacanti and Anthony Atala are two of the inventors on the instant application and are also two of the co-authors of Reference R.

4. Alan B. Retik is the third co-author of Reference R. Dr. Retik is not an inventor of the claimed invention.

5. Linda G. Griffith, Charles A. Vacanti, Keith T. Paige, and Anthony Atala mutually conceived and reduced to practice the invention recited in the claims of the '945 application. Dr. Griffith has changed her name from Griffith-Cima since the parent application was filed.

6. To the extent that Reference R discloses the claimed invention, the authors of Reference R derived this subject matter from us, the inventors of the '945 application. Dr. Retik's co-authors on Reference R communicated the subject matter of the claimed invention to Dr. Retik in connection with preparing Reference R. The authors of Reference R are not the inventors of the subject matter of the '945 application.

7. All statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents issued thereon.

  
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Anthony Atala, M.D.

12-7-01  
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Date

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Linda G. Griffith, Ph.D.

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Date

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Charles A. Vacanti, M.D.

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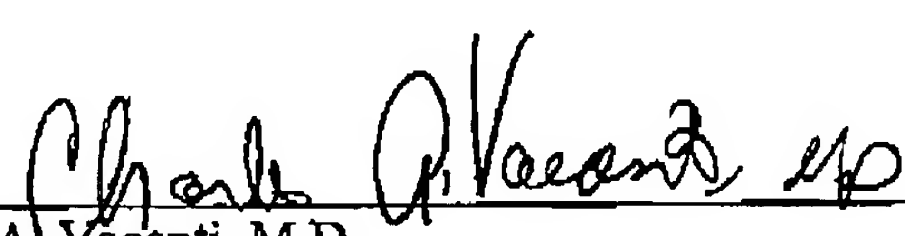
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*In re Stompel*, 113 USPQ 77(CCPA1957) and establishes conception and reduction to practice of the invention in this country before October 10, 1992.

3. The inventors of the claimed subject matter of United States Patent Application Serial No. 09/008,945 are Linda G. Griffith, Anthony Atala, Charles A. Vacanti, and Keith T. Paige. Dr. Griffith has changed her name from Griffith-Cima since the parent application was filed.


4. On a date before October 10, 1992, we conceived and reduced to practice our invention of a cell-polymeric composition for introducing cells into an animal.

5. Exhibit 1 is a copy of two pages from the laboratory notebook of Anthony Atala, with dates blacked out. Exhibit 1 provides evidence of conception and actual reduction to practice prior to October 10, 1992 of the claimed invention. In particular, page 1 bears notations describing how to combine chondrocytes with alginate. Page 2 describes how the chondrocyte/alginate suspension was injected to specific sites in a mouse to form cartilage tissue. The notes were prepared in the United States of America. The originals of these two pages bear dates prior to October 10, 1992.


7. Exhibit 2 is a typed transcript of the handwritten notes in Exhibit 1. Exhibit 2 is a complete and true transcript of the text of Exhibit 1.

8. All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents issued thereon.



  
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Anthony Atala, M.D.

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Linda G. Griffith, Ph.D.


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Date

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Charles A. Vacanti, M.D.

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Date

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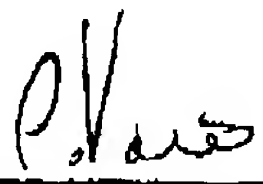
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Unchaineds → Bovine

cell count → [ ] to 10,000,000/cc Media

When ready to inject, fill Tapered 1715 / the glass  
or 1/2 Aljanta in it. → no needle on it  
on other 3 cc syringe → 1 cc to cell 1st.  
Draw a needle from cell 1st, 1st to Tapered  
1715 - immediately the pot another 1/2 needle  
on Tapered 1715 mix 1/2 inject. Quinich

2/12 T 9 cc of powder → ~~draw~~ 1/2 cc of 1715  
fill to 2/12 T 9 cc of 1715

Whole volume injected was 1/2 cc

Is a 50/50 mixture.

1715 lines 5,000,000 cc 10,000,000 cc 20,000,000 cc

1/2 cc

1/2 cc

1/2 cc

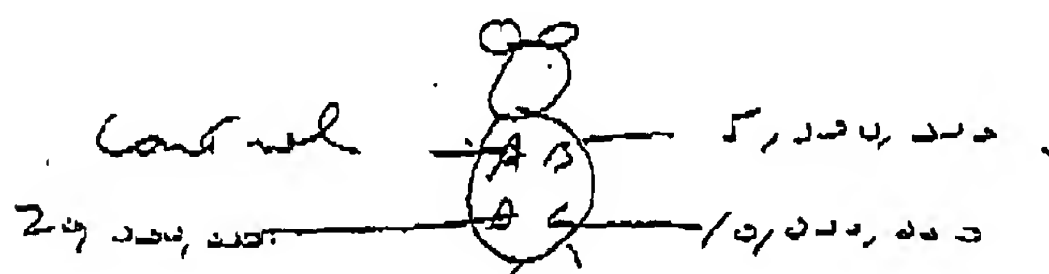


Exhibit 1

→ placed 0.1 cc of alginate (sterilized) in a Trencher's syringe -  
when pushed in loosely it was about 0.2 cc in volume.  
Drew syringe out to 0.5 cc. and kept as is.

→ Calculated suspension had =  $5,000,000 \text{ cells per cc} \times \frac{20 \text{ cc}}{100 \text{ cc}} = 100,000,000 \text{ cells total}$   
Calculated ~~the~~ added 5 cc of media =  $20,000,000 \text{ cells/cc}$   
(→ 3 cc of  $20,000,000 \text{ cells/cc}$ )  
Total 2 cc of suspension =  $40,000,000 \text{ cells total}$  - added 2 cc of  
(→ 4 cc of  $10,000,000 \text{ cells/cc}$ )  
Total 1 1/2 cc of susp =  $15,000,000 \text{ cells total}$  - added 1 1/2 cc.  
(→ 3 cc of  $5,000,000 \text{ cells/cc}$ ).

→ placed above 3 suspensions in 5 cc syringe.  
(bunches have been divided (12 each in Trencher's syringe & 0.3 cc each)  
also 1 sup of media only  
→ injected 0.3 cc of susp into Trencher's syringe - when  
it was injected it was 181 needles.



Transcript

Page 1

Chondrocytes-Bovine Cell count concentrated to ten million cells per cc of media.

When ready to inject, fill tuberculin syringes / take plunger out with alginate in it, no needle on it.

On another 3 cc syringe, place one cc of cell suspension.

Stick a needle from cell suspension syringe to tuberculin syringe. Immediately place another nineteen gauge needle on tuberculin syringe. Mix and inject quickly.

2/10 of a cc of powder, should be loose, not tight. Fill to 2/10 of a cc.

Whole volume injected was 0.5 cc.

So this is a 50/50 mixture.

Concentrations injected per 0.5 cc were 5 million, 10 million, and 20 million cells.

A diagram of a mouse showing the injection sites of 5, 10, and 20 million cells as well as a control site.

Exhibit 2